

THERAPEUTIC MANAGEMENT OF BOVINE CUTANEOUS PAPILLOMATOSIS WITH IVERMECTIN IN FARM BRED CALF CROPS OF WEST BENGAL, INDIA

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ABSTRACT: Incidence of infectious bovine cutaneous papillomatosis in farm bred calf crops of tropical West Bengal during 2008-2010 and its successful therapeutic management with injectable Ivermectin is reported. Diagnosis was based on clinicopathology and histopathological findings and effects of parenteral Ivermectin were clinically evaluated in 36 calves where Ivermectin was administered @ 1ml/50 kg body wt. by subcutaneous route for 3 occasions at 15 days interval. Hundred percent clinical recovery (n = 36) was observed in treatment group whereas persistence as well as different stages of papillomatous growth without regression or self cure was observed in (n = 10) control group.

Key words: Bovine papillomatosis, Warts, Ivermectin, Calves.

INTRODUCTION

Bovine papillomatosis is contagious in animals in which it naturally occurs and is caused by six different serotypes of epitheliotropic Bovine papilloma viruses (BPVs) having double stranded DNA as viral genome distinguished by their restriction endonuclease cleavage. Amongst the cutaneous affections as encountered in bovine calf crops, benign cutaneous neoplasm (tumours) or warts caused by BPVs forms a most common clinical entity. It can be defined as benign nodular lesions, finger like projections or cauliflower like small growths on the skin arising from stratified squamous epithelium. It may be single (solitary) or appear in multiples. The common sites for the development of cutaneous warts are head, eyelids, ears, neck, dewlap, brisket, shoulders and legs, occasionally on the back,

para-genital region and along the lower line of abdomen (Miller and West 1972, Smith 1996, Aiello 1988). Different methods have been used to treat bovine papillomatosis with varying success and although numerous cases of bovine papillomatosis have occurred among different breeds of bovine calf populations in West Bengal over past years documented data regarding diagnosis and treatment are still scarce. Thus, in order to obtain a better insight into bovine cutaneous papillomatosis (warts) in Indian calf crops, we report here incidences of recently observed cutaneous papillomatosis in organized dairy farms of West Bengal, based on clinical consideration of wart lesions, histopathological studies and treatment with parenteral Ivermectin for clinical recovery of the affected calves.

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MATERIALS AND METHODS

Survey of bovine papillomas with special emphasis to screening of cutaneous papillomatosis in calves was conducted in organized dairy farms and Goshalas located in new alluvial soil zone of tropical West Bengal, precisely in the districts of Nadia, North 24 Parganas and Howrah. Diagnosis of bovine papillomatosis was arrived at, on the basis of exhibited clinical signs, *i.e.* the papillomatous lesions ranging from 0.5 to 30 mm., solitary warts or with multiple papillomas disseminated on the head, ears, eyelids, around eyes, neck, shoulder, limbs, trunk and paragenital region. Since the structure of papillomas on the skin was easily observed and identified, clinical assessment and or clinical diagnosis was very much easy.

Clinically, 46 calves of different breeds, age, sex and weight, were histopathologically diagnosed as cutaneous papillomatosis, formed the materials of our studies. Thirty one (31) of these calves were male (age distribution varied 12 weeks to 40 weeks, average 6.5 months old) and remaining female 15 (fifteen) in numbers (age distribution varied 16 weeks to 48 weeks, average 8 months of age). Injectable Ivermectin (Trumectin® Zydus AHL and Neomec® - Intas) as per availability was administered to 36 calves ($n=36$) forming treatment group by subcutaneous route at the dose rate of 1ml/50 kg body weight for 3 occasions at 15 days interval and clinical recovery was assessed till 90 days and rest 10 calves ($n=10$) forming control group received subcutaneous injection of normal saline @10ml to each at 15 days interval as per treatment mode. Clinical efficiency of treatment was monitored for six months.

Cutaneous warts biopsy materials were

aseptically collected from cow calves and representative specimens were fixed in 10% formalin for histopathological studies.

HISTOPATHOLOGY

After proper fixation tissues were cut into small sections with thickness of 2-3mm, processed in ascending grades of alcohol for dehydration and cleared in benzoin .The paraffin embedded tissues were cut into 5 micron thin section and stained with Haematoxylin and Eosin (H&E) and examined by light microscopy.

RESULTS AND DISCUSSION

A total 46 cases of bovine cutaneous papillomatosis exhibited in 31 male calves and 15 female calves were studied. In the present study, clinically low to moderate number of warts were observed in head, eyelids, ears, neck, brisket, shoulder, thorax, limbs, para-genital area and ventral abdomen. Topographic specificity and regional distribution of warts as studied revealed dissemination of warts covering antero-dorsal part of the body with highest frequency (76.09%) (Fig.1) as compared to posterior and posterior ventral part of the body, with a low frequency (19.56%). However, extensive generalized papillomatosis or whole body papillomatosis were recorded in 4.35% cases.

In the present study, 100% success was obtained from the treatment of bovine papillomatosis with parenteral Ivermectin therapy in mixed breed of calf crops including cross bred calves and no reoccurrence was observed in treatment group during 6 months follow up examination. Complete clinical cure or total healing, regression or sloughing of warts occurred during 45 to 90th days post

Table 1 : Survey of naturally occurring warts and histopathological findings.

Name of the farm	No. of calves affected	History and gross observation	Histopathological observation
State Livestock Farm, Kalyani, Nadia, West Bengal	Male calves 12 Female calves – 3	Prevalence of cutaneous papillomas (CP) as known to occur in Jersey and Holstein cross bred calves, moderate number of warts were seen in head, neck, ears, eyelid, around eyes, muzzle, forelimbs, brisket and thorax.	Finger like projections covered by hyperplasia of epidermis, connective tissue structure showed engorged blood vessels and lymphocytic infiltration.
Haringhata Farm, Nadia, West Bengal	Male calves – 4 Female calf – 1	Hard typical pedunculated and non-pedunculated, horny solid warts were recorded in Gir and Sahiwal calves. Few warts were seen on head, ear base, ear pinna, around eyes, eyelid, face, body and thorax.	Hyperplasia of epidermal basal cells, moderate acanthosis, hyperkeratosis and parakeratosis.
Pinjrapole society Gaushala, Anandanagar, Kalyani, Nadia. West Bengal.	Male calves – 6 Female calves - 2	Warts with various stages of development were recorded in zebu calves and cross jersey calves. Moderate to extensive papillomatous lesions (3mm to 30mm size) were seen in head, neck, thorax, hind limbs, trunk and para-genital region, whole body papillomatosis in one case was also recorded.	Histopathologically revealed fibropapillomas with acanthosis, hyperkeratosis and down growth of rate ridges.

Name of the farm	No. of calves affected	History and gross observation	Histopathological observation
Pinjrapole society gousahala, Shodepur, North 24 Parganas, West Bengal	Male calves – 3 Female calves – 3	Rough surfaced, spiny warts were recorded in zebu calves and cross breed calves, moderate number of warts were present on head, neck and limb, thorax, abdomen and body, limb, thorax, abdomen in one case of ventral abdomen and paragenital area.	Histological analysis revealed epithelial hyperplasia, acanthosis and hyperkeratosis.
Pinjrapole society Gousahala, Uluberia, Howrah, West Bengal	Male calves – 4 Female calves – 2	Unsightly rough, lobate or fungiform harsh warts were recorded both in Zebu and crossbred jersey (XJY) and Holstein Frisean (XHF) calves. Moderate number of warts were present on head, neck, face, ear, body and hind limbs.	Hyperplasia of epidermis, vacuolating cells were also seen in some of the keratinized area near the border of the finger like projections.
Dairy Herds, National Dairy Research Institute (NDRI) Eastern Region, Kalyani, Nadia, West Bengal	Male calve - 1 Female calves - 5	Warts were recorded in cross jersey calves. Few warts were seen in face, neck, back and barrel.	Prominent finger like projections covered by hyperkeratinized layers, hyperplasia of stratum spinosum. In connective tissue stroma, connective tissue proliferation along with dilation of blood vessels were seen.

Table 2 : Topographic distribution of papillomas on calves body.

Dissemination or distribution of warts (Topographic location)	Animal numbers	Severity of warts	Percentage	Total percentage anterior/ posterior part of the body % distribution
Only head (Cephalic domain)	2	Mild	4.34%	
Ears only (Ear base and pina)	4	Mild	8.7%	
Eye lid and around eyes	5	Mid to moderate	10.82%	Mild to moderate warts
Only forelimbs (unilateral and bilateral)	5	Moderate	10.82%	76.09%
Head, neck and around eyes	6	Moderate	13.04%	
Head, neck and thorax	3	Moderate	6.54%	(Anterior or cranial part of the body)
Head, neck, face, muscle and fore limbs	5	Moderate	10.82%	
Brisket, neck and thorax	3	Mild to moderate	6.54%	
Head, neck and forelimbs	2	Mild to moderate	4.34%	
Back (Trunk) posterior lumber and on tail base	3	Mild	6.54%	Mild to moderate warts
Para-genital region	2	Mild to moderate	4.34%	19.56%
Ventral (lower) abdomen	1	Mild	2.17%	(Posterior part of the body)
Only hind limbs (unilateral/bilateral)	3	Moderate	6.54%	Extensive warts
Whole body papillomatosis (Extensive lesion)	2	Extensive	4.34%	4.34% (whole body distribution)

administration of Ivermectin. Healing was evaluated by macroscopic examination (decrease in diameter, color changes, dryness and dropping of dead tissue) where three (n: 3) calves (8.33%) in treatment group (1) at 45th day, seven (n : 7) calves (19.44%) at 60th day, twenty (n : 20) calves (54.44%) at 85th day and

further six (n : 6) calves (16.66%) at 90th day showed complete remission. However, none of the calves from control group, Gr.-II revealed remission rather exhibited warts progression at various stages of development with unsightly appearance and distressing to animals.

Our study clearly indicates that bovine

Table 3 : Animals showing clinical recovery in treatment group and control group.

Group	No of animals	Days						
		0	15	30	45	60	75	90
Gr. I	n = 36	-	-	-	3	7	20	6
Gr. II	n = 10	-	-	-	-	-	-	-

cutaneous papillomatosis is widely prevalent in West Bengal, affecting a good number of young calves even in organized dairy farms causing significant clinical entity and economic losses. Microscopic changes typical of fibropapillomas were observed in all cases of cutaneous papillomas revealing epidermal hyperplasia, acanthosis and hyperkeratosis along with



Fig. 1: Showing cutaneous warts (papillomus) in antero-dorsal part of bovine calf.

elongated growth of papillary projections extending into dermis (Fig.2 to 4). Similar changes were also observed by Abu-Samra *et al.* (1982), Gupta *et al.* (1989) and Sharma *et al.* (2003). Although there are many treatment modalities for warts remedy or regression, no

agreement has been achieved on the method to be used for the treatment of papillomas with

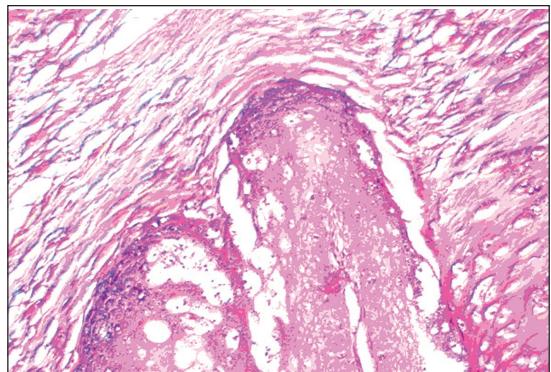


Fig.2: Cross section of cattle cutaneous wart showing degenerative changes of the cells of the rete pegs and marked cytoplasmic vacuolation of the rest of the cells, Fibropapilloma (H&EX 250).

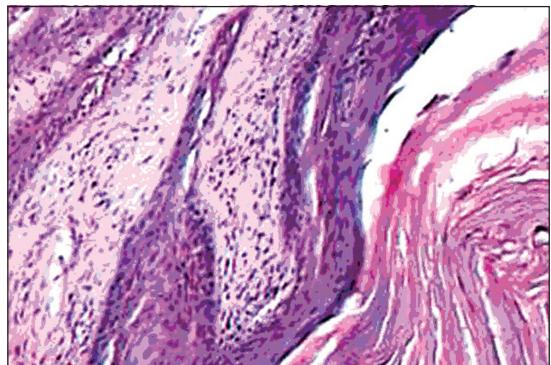


Fig.3: Finger like projection with excessive cornification, hyperplastic St. Spinorum and connective tissue core, Fibropapilloma (H&E X 100).

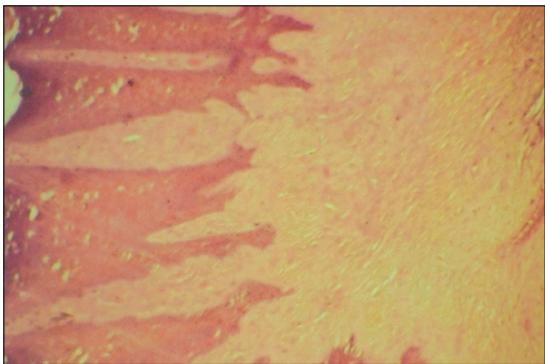


Fig.4: Cross section of cattle cutaneous wart showing oedema between St. Germinativum and rete pegs, marked rete pegging showing down proliferation in St. Spinosum. Fibropapilloma (H&E X 100).

sure success (Cimtay *et al.* 2003). Venugopalan (2000) and O'Connor (2001) have suggested remedial measures for removal of warts such as use of autogenous vaccine, wart enucleation, burning with hot iron or eraser, ligation and surgical removal of wart (excision) with surgical knife, application of salicylic acid ointment, dimethyl sulfoxide ointment and potential caustics etc. Autohaemotherapy of the affected calves were also tried (Pattanayak 2004).

Medicinal treatment with Anthiomaline, Antimosan, Fowler's solution, thuja (Homeopathic medicine) etc. are in practice but results are not always satisfactory. Now-a-days uses of some drugs causing non-specific immune stimulation have been found promising in clinical recovery or regression of warts. 100% success was achieved in the treatment of bovine papillomatosis with Levamisole (Cihan *et al.* 2004). In the present study, hundred percent clinical recovery was obtained while treating warts or cutaneous papillomatosis in calves with three consecutive dose of Ivermectin

administration by subcutaneous route (S/C) at 15 days interval at its normal dose rate *i.e.* 1ml/ 50 kg body weight. Regression or healing of warts could have occurred due to immune modulatory and antitumor effect of Ivermectin. Avermectins are derivatives of the fermentation products of the soil microorganisms which have got some antibiotic and pronounced anti-tumor activity (Drinayaev *et al.* 2004). To our knowledge, the usage of Ivermectin for the treatment of papillomatosis in cattle has been poorly studied but it is found promising in treating bovine cutaneous papillomatosis with 100% efficacy and that could possibly by non-specific immune induction *i.e.* both cellular and humeral immune function and inhibiting tumour progression by its inherent antitumor effect. Our findings were consistent with Borku *et al.* (2007) and Drinayaev *et al.* (2004), where Ivermectin had been used for the medication against viral papillomatosis or virus induced warts. Hence, it can be concluded that usage of Ivermectin is safe and cheap alternative treatment option for papillomatosis in calves in place of surgical or cryosurgical approaches (Cihan *et al.* 2004, Venugopalon 2000, Olson 1993 and Smith 1996).

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